



## DIETARY HABITS AND STOMACH CANCER IN SHANGHAI, CHINA

Bu-Tian Ji<sup>1,2\*</sup>, Wong-Ho CHOW<sup>1</sup>, Gong YANG<sup>2,3</sup>, Joseph K. McLAUGHLIN<sup>4</sup>, Wei ZHENG<sup>2,5</sup>, Xiao-Ou SHU<sup>2,6</sup>, Fan JIN<sup>2</sup>, Ru-Nie GAO<sup>2,7</sup>, Yu-Tang GAO<sup>2</sup> and Joseph F. FRAUMENI, JR.<sup>1</sup>

<sup>1</sup>Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA

<sup>2</sup>Department of Epidemiology, Shanghai Cancer Institute, Shanghai, People's Republic of China

<sup>3</sup>Zhejiang Cancer Institute, Zhejiang Medical University, Hangzhou, People's Republic of China

<sup>4</sup>International Epidemiology Institute, Rockville, MD, USA

<sup>5</sup>Division of Epidemiology, University of Minnesota, School of Public Health Minneapolis, MN, USA

<sup>6</sup>Division of Pediatric Epidemiology-Clinical Research, University of Minnesota, Minneapolis, MN, USA

<sup>7</sup>Health Status Section, Health Statistics Division, Statistics Canada, Ottawa, Canada

Stomach cancer remains the second leading cancer in incidence in Shanghai, China, despite its decline over the past 2 decades. To clarify risk factors for this common malignancy, we conducted a population-based case-control study in Shanghai, China. Included in the study were 1,124 stomach cancer patients (age 20–69) newly diagnosed in 1988–1989 and 1,451 controls randomly selected among Shanghai residents. Usual adult dietary intake was assessed using a comprehensive food frequency questionnaire. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression models. Risks of stomach cancer were inversely associated with high consumption of several food groups, including fresh vegetables and fruits, poultry, eggs, plant oil, and some nutrients, such as protein, fat, fiber and antioxidant vitamins. By contrast, risks increased with increasing consumption of dietary carbohydrates, with odds ratios (ORs) of 1.5 (95% confidence interval [CI] 1.1–2.1) and 1.9 (95% CI 1.3–2.9) in the highest quartile of intake among men ( $p$  for trend = 0.02) and women ( $p$  = 0.0007), respectively. Similar increases in risk were associated with frequent intake of noodles and bread in both men ( $p$  = 0.07) and women ( $p$  = 0.05) after further adjustment for fiber consumption. In addition, elevated risks were associated with frequent consumption of preserved, salty or fried foods, and hot soup/porridge, and with irregular meals, speed eating and binge eating. No major differences in risk were seen according to subsite (cardia vs. non-cardia). Our findings add to the evidence that diet plays a major role in stomach cancer risk and suggest the need for further evaluation of risks associated with carbohydrates and starchy foods as well as the mechanisms involved. *Int. J. Cancer* 76:659–664, 1998.

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Stomach cancer is the second leading malignancy following lung cancer among men and breast cancer among women in Shanghai, with age-standardized annual incidence rates of 50.1 and 23.2/100,000 in 1987–1989, respectively (Jin *et al.*, 1993). The rates have declined substantially over the past 2 decades, as in Western societies, indicating the importance of environmental exposures (Nomura, 1996). To clarify risk factors for this common cancer, we conducted a large population-based case-control study in urban Shanghai. In a previous analysis, cigarette smoking was shown to elevate the risk of cardia and non-cardia gastric cancers (Ji *et al.*, 1996). In the present study, we examine the role of dietary practices.

### MATERIAL AND METHODS

The materials and methods for this study have been described in detail elsewhere (Ji *et al.*, 1996). Briefly, stomach cancer patients, aged 20–69, newly diagnosed between December 1, 1988 and November 30, 1989, were identified among permanent residents of the 10 urban districts of Shanghai. Of the 1,722 eligible patients, 353 (20.5%) died before interview, 153 (8.9%) moved away, 19 (1.1%) refused to participate and 73 (4.2%) were excluded because only clinical diagnostic information was available. Of the 1,124

(770 men and 354 women) patients (65.3%) included in the analysis, 52.1% were confirmed by histology and 47.9% by other diagnostic methods including surgery, endoscopy, X-ray and ultrasound. Controls were selected among permanent residents of Shanghai, frequency matched to the expected distributions of cases by age (5-year category) and sex. Of the 1,692 eligible controls randomly selected from the Shanghai Resident Registry files, 1,451 (819 men and 632 women) were interviewed, yielding a response rate of 85.8%.

Each subject was interviewed in person by trained interviewers. A structured questionnaire elicited information on demographic and socio-economic conditions, diet, cigarette smoking, alcohol drinking, history of selected diseases, family history of cancer, occupation and other factors. Questions on dietary factors included preference for selected cooking methods and eating habits, as well as usual food intake 10 years before diagnosis for cases or before the date of interview for controls. Frequency and amount of intake for 74 commonly consumed food items and frequency of intake of 10 preserved items were obtained. These items account for over 80% of food intake in Shanghai residents. Consumption of seasonal vegetables and fruits was assessed on the basis of average intake during the relevant period of the year. Frequency of intake of selected food groups was examined by combining related food items (Table I). Since few individual food items had missing values on the frequency of intake (only 19 subjects had 1–2 missing values from the 74 food items and 20 subjects had 1–7 missing values from preserved food items), they were treated as zero intake when being summed into a food group. Quantitative estimates of nutrients in each food were based on food tables derived from the Chinese Food Composition Tables (Chinese Academy of Medical Sciences, 1991). Total intake of each nutrient was summed over all foods consumed.

Continuous variables of food or nutrient intake were divided into quartiles based on the distribution among controls, with approximately equal number of controls in each intake stratum. While the frequency of intake of food items and groups was similar between men and women, the amount of intake varied substantially between the sexes. Hence sex-specific cutpoints were used for amount of nutrient intake (see Appendix I for cutpoints for food groups and Appendix II for nutrient intake). Risk of stomach cancer associated with dietary factors was estimated by odds ratios (ORs) and 95% confidence intervals (CIs), using unconditional logistic regression models (Breslow and Day, 1980). Dose-response relations were examined by test of linear trends on categorical variables. All ORs were adjusted for age, monthly family *per capita* income and educational level. In addition, ORs for men were further adjusted

\*Correspondence to: National Cancer Institute, 6130 Executive Blvd, EPN 415, Rockville, MD 20852, USA. Fax: (301) 402-1819.  
E-mail: jib@epndce.nci.nih.gov

TABLE I – FOOD GROUPS

Food groups	Description
Preserved vegetable foods	Salted moldy dried vegetables, salted vegetables, hot pickled mustard stem, fermented bean-curd
Preserved animal foods	Cured meat, sausages, salted egg, preserved limes duck eggs, salted pork, salted fish
Red meats	Pork chops, pork spareribs, pig feet, fresh pork (fat, lean or combination), beef, mutton
Organ meats	Pork liver, chicken liver, other animal organs
Poultry	Chicken, duck
Fresh fish	Sea fish, fresh water fish, eel, shrimp, crab
Eggs	Eggs, excluding salt or other preserved eggs
Rice	Any rice
Noodles and bread	Noodles, bread/steamed bun
Yellow/green vegetables	Shanghai bok choy, Chinese cabbage, spinach, peapods, green peas, green beans, green broad beans, red and green peppers, carrots, sweet potatoes
Cruciferous vegetables	Shanghai bok choy, cabbage, Chinese cabbage, cauliflower, radish (white)
Allium vegetables	Onion/garlic, Chinese chives
Soybean products	Soy bean milk, bean curd, fried bean curd, other bean products
All vegetables	Shanghai bok choy, spinach, cabbage, Chinese cabbage, cauliflower, celery, bean sprouts, eggplant, wild rice stem, pea pods, green peas, green beans, green broad beans, celtuce, sweet potatoes, white gourd, cucumber, radish (white), carrots, mushrooms, red and green peppers, tomato, bamboo shoot, lotus root, luffa or sponge gourd, onion and garlic, Chinese chives, ginger, kelp and seaweeds
Fresh fruit	Soy bean milk, bean curd, fried bean curd, other bean products
Plant oil	Apple, pea, orange and tangerine, water melon, banana
Animal fat	Rapeseed oil, bean oil, sesame oil
	Lard

for cigarette smoking and alcohol drinking, confounding factors that are common among Chinese men but not among Chinese women (only 8% of women smoked, and 3% drank alcohol regularly). ORs for nutrients were adjusted for total caloric intake, using the standard method (Kipnis *et al.*, 1993) for micronutrients and the residual method (Willett and Stampfer, 1986) for macronutrients. Risks were assessed for all stomach cancers combined and by subsite (cardia and non-cardia).

## RESULTS

Compared with controls, patients were slightly older (median age 61 years for cases and 59 years for controls) and tended to have lower monthly income (41% of cases *vs.* 30% of controls with an average *per capita* income of 22 Chinese Yuan/month or less) and less education (61% of cases *vs.* 43% of controls with primary school or lower education). Among men, 18.8% of gastric tumors arose in the cardia, 68.9% in non-cardia stomach and 12.3% in an unclassified subsite. Among women, the corresponding distribution was 11.3%, 72.6% and 16.1%.

### Food groups

Intake of preserved foods, particularly preserved vegetables, was associated with an elevated risk of stomach cancer among women, but not men (Table II). Of the fresh animal food groups, poultry intake was inversely related to risk in both men ( $p$  for trend = 0.0005) and women ( $p$  = 0.15), with a 20–30% reduction in risk in the highest quartile of intake. Risk also was reduced 40–50% among those with the highest quartile of egg consumption ( $p$  for trend = 0.001 for men and 0.003 for women). No association was seen for fresh red meats, organ meats or fish.

Consumption of various fresh vegetables tended to be inversely related to risk, especially in the highest quartile of intake (Table II). However, significant trends were seen only for yellow-green vegetables, soybean and soy products and total vegetables among men, with the greatest reduction (60%) among those with the highest consumption of total fresh vegetables. No significant trends with vegetable intake were seen among women. Of all food groups, the risk reduction was most pronounced for fresh fruits. The ORs were 0.7, 0.7 and 0.4 in the 2nd, 3rd and 4th quartiles of intake among men ( $p$  < 0.0001); and 0.7, 0.6 and 0.5 in the corresponding quartiles among women ( $p$  = 0.0006).

Little variation was seen in the frequency of rice consumption in this population, hence only 2 levels of intake were formed (Table

II). No association was apparent with intake of rice or noodles/bread. Animal fat was not associated with risk, but intake of plant oil significantly reduced the risks in both men ( $p$  = 0.001) and women ( $p$  = 0.005).

Subsite analyses revealed no consistent or statistically significant differences in risk between cardia and non-cardia tumors across levels of intake of food groups or food items (data not shown).

### Nutrients

Total caloric intake was inversely related to risk of stomach cancer among men ( $p$  = 0.002) but not women (Table III). In both men and women, risks declined significantly with increasing intake of protein and fats after further adjustment for caloric intake, while risks remained elevated with increasing carbohydrate intake. By contrast, intake of dietary fibers (mostly from carbohydrate-rich foods such as grains, fruits and vegetables) was inversely related to risks. Reduced risks were also associated with intake of several dietary vitamins examined in our study, including ascorbic acid, carotene, riboflavin, vitamin A and vitamin E.

Rice and noodles/bread are major sources of both carbohydrates and fibers. When adjusted for dietary fibers, the risks for noodles/bread resembled those for carbohydrates, with ORs among men of 1.2 (95% CI 0.8–1.6), 1.2 (0.9–1.6) and 1.5 (1.1–2.0) in the upper 3 quartiles, respectively ( $p$  for trend = 0.07). Among women, the corresponding ORs were 1.3 (0.9–1.9), 1.7 (1.1–2.4) and 1.5 (0.9–2.3;  $p$  for trend = 0.05). Given the homogeneity in frequency of rice intake in Shanghai (usually 3 meals a day), we estimated risks according to the amount of rice consumed per day. Similarly, after adjustment for dietary fibers, ORs were 1.3 (95% CI 0.9–1.9,  $p$  for trend = 0.5) and 1.8 (95% CI 1.1–2.5,  $p$  for trend = 0.07) in the highest levels of rice consumption among men (>600 gr/day) and women (>450 gr/day), respectively, relative to those in the lowest levels of intake (400 gr/day for men and 350 gr/day for women). By contrast, risks associated with intake of rice and noodles/bread were reduced slightly, but not significantly, after adjustment for carbohydrates. The excess risks associated with dietary carbohydrates and starchy foods were not substantially altered after further adjustment for birthplace (born in Shanghai *vs.* elsewhere) or intake of fresh vegetables and fruits and other selected dietary factors (data not shown).

Subsite analyses revealed no consistent or statistically significant differences in risk associated with nutrient intake across levels of intake (data not shown).

**TABLE II** – ODDS RATIOS<sup>1</sup> (OR) AND 95% CONFIDENCE INTERVALS (CI) OF STOMACH CANCER IN RELATION TO QUARTILES (Q) OF FOOD GROUP CONSUMPTION BY SEX, SHANGHAI, CHINA (1988–1989)<sup>2</sup>

	Men				<i>p</i> for trend	Women				<i>p</i> for trend
	Q1 (low)	Q2	Q3	Q4 (high)		Q1 (low)	Q2	Q3	Q4 (high)	
Preserved vegetable foods	1.0	0.9 (0.7–1.2)	1.0 (0.8–1.4)	0.9 (0.7–1.2)	0.54	1.0	1.7 (1.1–2.5)	1.9 (1.3–2.8)	1.9 (1.3–2.8)	0.002
Preserved animal foods	1.0	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.8 (0.6–1.0)	0.10	1.0	1.8 (1.3–2.7)	1.4 (0.9–2.0)	1.3 (0.9–2.0)	0.44
Fresh red meats	1.0	0.9 (0.7–1.2)	1.1 (0.8–1.4)	0.9 (0.6–1.2)	0.61	1.0	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.8 (0.6–1.2)	0.35
Organ meats	1.0	1.1 (0.8–1.4)	1.1 (0.8–1.3)		0.70	1.0	0.8 (0.6–1.2)	1.3 (0.9–1.7)		0.16
Poultry	1.0	1.0 (0.7–1.3)	0.6 (0.5–0.9)	0.7 (0.5–0.9)	0.0005	1.0	0.9 (0.6–1.4)	0.9 (0.6–1.3)	0.8 (0.5–1.1)	0.15
Fish	1.0	1.0 (0.7–1.3)	0.9 (0.7–1.2)	0.8 (0.6–1.1)	0.21	1.0	1.1 (0.8–1.6)	1.0 (0.7–1.5)	0.9 (0.6–1.3)	0.48
Eggs	1.0	0.8 (0.6–1.0)	0.9 (0.7–1.1)	0.6 (0.4–0.8)	0.001	1.0	1.0 (0.7–1.5)	0.8 (0.6–1.1)	0.5 (0.4–0.8)	0.003
All vegetables	1.0	0.7 (0.5–0.9)	0.7 (0.6–1.0)	0.4 (0.3–0.5)	<0.0001	1.0	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.7 (0.5–1.1)	0.09
Yellow/green vegetables	1.0	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.5 (0.4–0.7)	0.0001	1.0	0.7 (0.5–1.0)	0.9 (0.6–1.2)	0.7 (0.5–1.1)	0.08
Cruciferous vegetables	1.0	1.1 (0.8–1.4)	0.9 (0.7–1.2)	0.8 (0.6–1.1)	0.07	1.0	1.1 (0.8–1.6)	1.1 (0.7–1.5)	0.8 (0.5–1.1)	0.20
Allium vegetables	1.0	1.3 (0.9–1.7)	1.1 (0.8–1.5)	0.8 (0.6–1.1)	0.08	1.0	0.9 (0.6–1.3)	0.8 (0.6–1.2)	0.8 (0.5–1.2)	0.58
Soybean and products	1.0	0.9 (0.6–1.1)	0.7 (0.5–1.0)	0.5 (0.4–0.7)	0.0001	1.0	1.2 (0.9–1.7)	1.2 (0.8–1.8)	0.8 (0.5–1.1)	0.26
Fresh fruits	1.0	0.7 (0.5–0.9)	0.7 (0.5–0.9)	0.4 (0.3–0.6)	<0.0001	1.0	0.7 (0.5–1.1)	0.6 (0.4–0.9)	0.5 (0.3–0.8)	0.0006
Rice	1.0	1.0 (0.8–1.3)				1.0	1.2 (0.7–2.0)			
Noodles and bread	1.0	1.1 (0.8–1.5)	1.0 (0.8–1.4)	1.1 (0.9–1.5)	0.38	1.0	1.2 (0.9–1.7)	1.4 (1.0–2.0)	1.2 (0.8–1.8)	0.13
Animal fat	1.0	1.6 (1.0–2.5)	1.5 (1.1–1.9)	1.0 (0.8–1.3)	0.44	1.0	1.2 (0.6–2.5)	0.9 (0.7–1.4)	1.2 (0.9–1.7)	0.20
Plant oil	1.0	0.8 (0.6–1.1)	0.6 (0.4–0.8)	0.7 (0.5–0.9)	0.001	1.0	0.9 (0.6–1.3)	0.6 (0.4–0.9)	0.6 (0.4–0.9)	0.005

<sup>1</sup>Adjusted for age, income, education, smoking (males only) and alcohol drinking (males only).—<sup>2</sup>Data are ORs, with 95% CIs in parentheses.

**TABLE III** – ODDS RATIOS<sup>1</sup> (OR) AND 95% CONFIDENCE INTERVALS (CI) OF STOMACH CANCER IN RELATION TO QUARTILES OF NUTRIENTS BY SEX, SHANGHAI, CHINA (1988–1989)<sup>2</sup>

	Men				<i>p</i> for trend	Women				<i>p</i> for trend
	Q1 (low)	Q2	Q3	Q4 (high)		Q1 (low)	Q2	Q3	Q4 (high)	
Total calories	1.0	0.8 (0.6–1.0)	0.7 (0.5–1.0)	0.6 (0.5–0.8)	0.002	1.0	1.0 (0.7–1.5)	0.8 (0.5–1.2)	1.1 (0.7–1.6)	1.0
Protein	1.0	0.9 (0.7–1.2)	0.6 (0.5–0.9)	0.7 (0.5–0.9)	0.003	1.0	0.9 (0.6–1.3)	0.7 (0.5–1.0)	0.6 (0.4–1.0)	0.01
Fat	1.0	0.8 (0.6–1.1)	0.7 (0.5–1.0)	0.7 (0.5–1.0)	0.07	1.0	0.6 (0.4–0.9)	0.6 (0.4–0.9)	0.6 (0.4–0.8)	0.006
Carbohydrates	1.0	1.1 (0.8–1.5)	1.1 (0.9–1.6)	1.5 (1.1–2.1)	0.02	1.0	0.9 (0.6–1.4)	1.1 (0.7–1.7)	1.9 (1.3–2.9)	0.0007
Dietary fibers	1.0	1.2 (0.9–1.5)	0.9 (0.6–1.2)	0.6 (0.4–0.8)	0.002	1.0	0.8 (0.6–1.2)	0.6 (0.4–0.9)	0.6 (0.3–0.9)	0.007
Ascorbic acid	1.0	1.1 (0.8–1.4)	0.6 (0.5–0.8)	0.5 (0.3–0.7)	<0.0001	1.0	0.8 (0.6–1.2)	1.1 (0.8–1.7)	0.7 (0.5–1.1)	0.40
Carotene	1.0	0.7 (0.5–0.9)	0.6 (0.5–0.9)	0.4 (0.3–0.6)	<0.0001	1.0	1.2 (0.8–1.7)	0.7 (0.5–1.0)	0.7 (0.5–1.1)	0.02
Riboflavin	1.0	0.7 (0.5–0.9)	0.7 (0.5–0.9)	0.4 (0.3–0.6)	<0.0001	1.0	0.9 (0.6–1.3)	0.8 (0.5–1.2)	0.5 (0.3–0.9)	0.003
Vitamin A	1.0	0.9 (0.7–1.2)	0.8 (0.6–1.1)	0.7 (0.5–1.0)	0.02	1.0	1.1 (0.8–1.6)	0.8 (0.6–1.2)	0.8 (0.5–1.3)	0.22
Vitamin E	1.0	0.6 (0.4–0.7)	0.6 (0.5–0.8)	0.5 (0.3–0.7)	<0.0001	1.0	1.0 (0.7–1.4)	0.7 (0.5–1.1)	0.5 (0.3–0.8)	0.0002

<sup>1</sup>Adjusted for age, income, education, smoking (males only), alcohol drinking (males only) and total calories intake.—<sup>2</sup>Data are ORs, with 95% CIs in parentheses

### Eating preferences

Risks of stomach cancer rose with increasing frequency of intake of salted foods and preference for increasing saltiness (Table IV), particularly for non-cardia tumors (OR 1.8, 95% CI 1.3–2.7). In addition, risks for both cardia and non-cardia tumors increased

2-fold with frequent consumption of fried foods and declined 40–50% with frequent intake of raw and fresh foods. No association was found for smoked foods.

Several eating patterns were also associated with 2- to 4-fold excess risks, including preference for burning hot soup/porridge,

**TABLE IV** – ODDS RATIOS<sup>1</sup> (OR) AND 95% CONFIDENCE INTERVALS (CI) OF STOMACH CANCER IN RELATION TO PREFERENCE OF EATING HABITS BY SUBSITE OF STOMACH CANCER, SHANGHAI, CHINA (1988–1989)

	Control	Overall stomach			Cardia			Distal		
		Cases	OR	95% CI	Cases	OR	95% CI	Cases	OR	95% CI
Consume salted foods										
Occasionally	188	98	1.0		18	1.0		57	1.0	
Sometimes	1,079	843	1.4	(1.1–1.9)	135	1.2	(0.7–2.1)	502	1.5	(1.1–2.0)
Frequently	187	181	1.7	(1.3–2.4)	23	1.1	(0.5–2.0)	112	1.8	(1.3–2.7)
<i>p</i> for trend				0.001			1.0			0.002
Preference for saltines										
Low salty	1,022	717	1.0		114	1.0		431	1.0	
Somewhat	407	382	1.3	(1.1–1.6)	55	1.1	(0.8–1.6)	229	1.3	(1.1–1.6)
Very salty	11	18	2.3	(1.0–4.9)	6	4.3	(1.5–12.5)	7	1.5	(0.6–4.0)
<i>p</i> for trend				0.0005			0.10			0.008
Fried foods										
Occasionally	215	153	1.0		27	1.0		389	1.0	
Sometimes	1,143	838	1.1	(0.9–1.4)	130	1.0	(0.7–1.6)	515	1.2	(0.9–1.5)
Frequently	88	131	2.3	(1.6–3.2)	19	2.1	(1.1–4.1)	67	2.0	(1.3–3.0)
<i>p</i> for trend				0.0001			0.09			0.004
Smoked foods										
Occasionally	455	458	1.0		64	1.0		230	1.0	
Sometimes	968	704	0.9	(0.7–1.1)	110	0.9	(0.7–1.3)	423	0.9	(0.7–1.1)
Frequently	22	30	1.6	(0.9–2.8)	2	0.6	(0.1–2.8)	18	1.7	(0.9–3.2)
<i>p</i> for trend				0.53			0.55			0.79
Raw and fresh foods										
Occasionally	973	826	1.0		134	1.0		487	1.0	
Sometimes	270	192	0.9	(0.7–1.1)	26	0.7	(0.5–1.1)	121	0.9	(0.7–1.2)
Frequently	197	99	0.6	(0.5–0.8)	15	0.5	(0.3–1.0)	59	0.6	(0.4–0.8)
<i>p</i> for trend				0.0001			0.02			0.003
Hot soup or porridge										
Not hot	307	182	1.0		23	1.0		116	1.0	
Sometimes	843	597	1.2	(1.0–1.5)	90	1.4	(0.8–2.3)	346	1.1	(0.9–1.4)
Burning hot	281	330	1.9	(1.5–2.5)	61	2.9	(1.7–4.9)	200	1.9	(1.4–2.5)
<i>p</i> for trend				<0.0001			<0.0001			<0.0001
Irregular meals										
Never	1,123	661	1.0		112	1.0		391	1.0	
Somewhat	245	297	2.0	(1.6–2.4)	32	1.2	(0.7–1.8)	181	2.1	(1.7–2.6)
Frequently	71	159	3.6	(2.7–4.9)	31	4.0	(2.4–6.5)	95	3.7	(2.7–5.2)
<i>p</i> for trend				<0.0001			<0.0001			<0.0001
Speed of eating										
Moderate	614	312	1.0		34	1.0		206	1.0	
Slow	207	101	1.0	(0.7–1.3)	11	1.1	(0.5–2.2)	61	0.9	(0.7–1.3)
Fast	619	704	2.0	(1.8–2.5)	130	3.8	(2.5–5.7)	400	1.8	(1.5–2.2)
<i>p</i> for trend				<0.0001			<0.0001			<0.0001
Binge eating										
No	1,259	831	1.0		126	1.0		499	1.0	
Yes	175	280	2.5	(2.0–3.1)	48	3.0	(2.0–4.4)	164	2.4	(1.9–3.1)

<sup>1</sup>Adjusted for age, sex, income, education, smoking and alcohol drinking.

frequent irregular meals, fast eating and binge eating. The excess risks associated with preference for hot soup/porridge and speed eating were greater for cardia than non-cardia tumors (Table IV).

Further adjustment for other potential confounding factors, such as green tea drinking, physical activity, body mass index and occupation, did not affect the associations with food group and nutrient intakes. In addition, risks were consistent by diagnostic status of cases (pathologic confirmation *vs.* other methods of diagnosis) (data not shown). Information on the Laurén classification of pathology (diffuse *vs.* intestinal type) was not available for analyses in our study.

#### DISCUSSION

Dietary factors are generally considered to play a major role in gastric carcinogenesis (Nomura, 1996; WCRF, 1997). Most consistent has been the reduced risk associated with consumption of fresh vegetables and fruits, as we and others have observed (Buiatti *et al.*, 1989; Tuyns *et al.*, 1992; Hoshiyama and Sasaba, 1992; Lee *et al.*, 1995). Our study and others (La Vecchia *et al.*, 1994; Zhang *et al.*, 1997) have also suggested that the protective effect of vegetables and fruits is related in part to the concentration of antioxidant vitamins, which may block the intragastric formation of carcinogenic N-nitroso compounds (Mirvish, 1996). Similarly, the inverse

association we found with intake of total fat and plant oil (a main contributor to total fat) in this population may be related to the high content of vitamin E, another antioxidant (Mirvish, 1996). Our finding of an inverse association with dietary fibers was largely explained by the reduced risks associated with fruits and vegetables.

Other food groups associated with risk reduction in our study included poultry and eggs. In China, frequent consumption of poultry and to some extent eggs may be an indicator of affluent lifestyle, since poultry is considered superior to and is more expensive than other common animal foods. Likewise, eggs are often consumed as supplemental foods for their nutritional value. The inverse associations found for these food groups in our study, therefore, may be confounded by the relation of low socio-economic status to stomach cancer risk (Nomura, 1996). Although we adjusted for family income and educational levels, there may still be residual confounding by these variables or other unmeasured risk factors related to socio-economic status. The reduced risks associated with high intake of poultry and eggs also were reflected, in part, in the inverse association with protein consumption in our study. However, we did not find associations with intake of other animal foods, such as fresh red meats and fish. High consumption of fresh meats has been associated with reduced risks in some studies (Hirayama, 1971), while others have reported a



positive association (Buiatti *et al.*, 1989; Wu-Williams *et al.*, 1990; Ward *et al.*, 1997).

By contrast, high intake of preserved animal and vegetable foods has been consistently linked to stomach cancer risk (You *et al.*, 1988; Hoshiyama and Sasaba, 1992; Lee *et al.*, 1995). These foods contain high levels of N-nitroso compounds and salt, which are believed to play a role in gastric carcinogenesis. The increased risks we observed with high intake of preserved foods, particularly preserved vegetables among women, and with salted foods in both sexes are consistent with previous observations (Tuyns, 1988; Buiatti *et al.*, 1989; Hoshiyama and Sasaba, 1992). By contrast, we found no significant association with consumption of smoked foods, suggesting that the salt and nitrates/nitrites used for food preservation rather than preserved foods *per se* are the likely risk factors.

A positive association with dietary carbohydrates or starchy foods has been reported in several studies of stomach cancer (Risch *et al.*, 1985; La Vecchia *et al.*, 1987; You *et al.*, 1988; Tuyns *et al.*, 1992; Hoshiyama and Sasaba, 1992), but not in others (Jacobs *et al.*, 1995). The excess risk associated with starchy foods such as rice and noodles/bread in our study could not be explained by education, income, birthplace, intake of fresh vegetables and fruits or other dietary factors, although residual confounding by these or other unmeasured variables remains possible. The mechanism by which high consumption of carbohydrates accompanied by low protein intake may increase the risk of stomach cancer is unclear, but several possibilities have been suggested, including physical irritation (especially from rough whole-grain cereals), reduction in gastric mucin, and lowering of gastric pH with promotion of acid-catalyzed nitrosation (Nomura, 1996).

Increased risks of stomach cancer have been linked to elevated consumption of high-temperature cooked foods in some studies (Hoshiyama and Sasaba, 1992; Ward *et al.*, 1997), but not all (Lee *et al.*, 1995; Zhang *et al.*, 1997). High-temperature cooking of foods, particularly meats, produces a variety of mutagenic and carcinogenic compounds that may promote the development of colon and other cancers (de Meester and Gerber, 1995). The moderately elevated risk associated with frequent consumption of fried foods in our study seems consistent with a role for pyrolysis compounds in gastric carcinogenesis, but further studies are warranted.

Our study also suggested that eating habits may be linked to excess gastric cancer risk, including preference for burning hot soup/porridge, frequent irregular meals, fast eating, and history of binge eating. While consumption of foods at high temperature has been linked to stomach cancer in one case-control study (La Vecchia *et al.*, 1990), other eating habits have seldom been examined. Since these variables may be especially prone to recall bias, further studies are needed, particularly in other populations.

In a few studies of stomach cancer that examined dietary associations by anatomic subsite, the risk patterns were similar for cardia and non-cardia tumors (Wu-Williams *et al.*, 1990; Zhang *et al.*, 1997). Although our results for food groups and nutrients are consistent with these earlier reports, we found that salted foods

were mainly related to non-cardia cancer, while preference for burning hot soup/porridge or fast eating were mainly linked to cardia cancer. Given the divergent incidence trends for cardia and non-cardia gastric cancers in some populations (Blot *et al.*, 1991), further study of the dietary associations by subsite appears warranted.

Although our findings are consistent with most previous studies of stomach cancer, several potential limitations of our study should be noted. While the participation rate among the controls was relatively high (86%), only 65% of the eligible cases participated. Since there was generally a 1-month delay between diagnosis and interview for cases, a few (9%) had moved away and could not be traced. The main reason for non-participation among cases was death (21%), thus raising the possibility of survival bias. If the identified risk factors also affected survival from stomach cancer, then exclusion of deceased cases may underestimate the true risks associated with these factors. On the other hand, selection bias, which tends to shift the risk estimates away from unity, should be minimal since only a small percentage of subjects refused to participate. Efforts were made to minimize potential recall bias in various ways, including extensive training of interviewers, use of a standardized questionnaire and ascertainment of usual diet 10 years prior to interview. While 48% of the cases were diagnosed by methods other than histological confirmation, exclusion of these cases did not alter our main findings.

Certain variables relevant for gastric cancer etiology were not collected in our study, including carriage of *Helicobacter pylori* and Laurén classification of histologic type. Although *H. pylori* infection is an established risk factor for stomach cancer in many populations (IARC, 1994), a prospective study in Shanghai was not able to detect an association (Webb *et al.*, 1996), so that a confounding or modifying effect would be difficult to detect. While it has been suggested that certain dietary associations vary between diffuse vs. intestinal tumors (Harrison *et al.*, 1997), dietary data by the Laurén classification are limited, and our study was not able to shed light on this issue.

In conclusion, our population-based case-control study of stomach cancer in Shanghai confirmed previous reports of protective effects associated with high consumption of fresh vegetables and fruits and a number of antioxidant vitamins, and elevated risks associated with high intake of preserved and salted foods. The positive association seen with intake of carbohydrates and starchy foods warrants further investigation in other populations. Relationships to food groups and nutrients were generally similar for cardia and non-cardia tumors of the stomach. Our findings provide further evidence that diet plays a major role in the development of stomach cancer and indicates the need for additional research to clarify the risks associated with carbohydrate and starchy foods, as well as the mechanisms involved.

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APPENDIX I – CUTPOINTS FOR QUANTILES OF SERVINGS OF FOOD GROUP PER MONTH

Food group/item	Quartile			
	Q1 (low)	Q2	Q3	Q4 (high)
Preserved vegetable foods	≤4.3	4.4–9.5	9.6–19.1	≥19.2
Preserved animal foods	≤1.8	1.9–4.5	4.6–10.3	≥10.4
Fresh red meats	≤8.5	8.6–16.1	16.2–30.6	≥30.7
Organ meats	0	0.1–0.9	≥1	
Poultry	≤0.7	0.8–1.4	1.5–2.4	≥2.5
Fish	≤6.0	6.1–10.7	10.8–17.3	≥17.4
Eggs	≤4.3	4.4–12.7	12.8–17.4	≥17.5
All vegetables	≤158.9	159.0–210.4	210.5–263.4	≥263.5
Yellow/green vegetables	≤77.3	77.4–98.6	98.7–123.0	≥123.1
Cruciferous vegetables	≤37.6	37.7–48.1	48.2–59.9	≥60.0
Allium vegetables	≤0.9	1.0–3.0	3.1–8.5	≥8.6
Soybean and products	≤7.5	7.6–12.8	12.9–23.3	≥23.4
Fresh fruits	≤1.6	1.7–6.0	6.1–18.0	≥18.1
Rice <sup>1</sup>	<90	≥90		
Pasta/bread	≤4.2	4.3–9.9	10.0–25.7	≥25.8
Animal fat (g/m)	0	0.1–31.3	31.4–83.3	≥83.4
Plant oil (g/m)	≤266.7	266.8–470.0	470.1–611.1	≥611.2

<sup>1</sup>Quartiles were not available for frequent intake of rice.

APPENDIX II – CUTPOINTS FOR QUANTILES OF NUTRIENT INTAKE PER DAY (BY SEX)

Nutrients (unit)	Quartile			
	Q1 (low)	Q2	Q3	Q4 (high)
Total calories (kcal)				
Men	≤2394.5	2394.6–2768.7	2768.8–3216.7	≥3216.8
Women	≤1862.8	1862.9–2214.5	2214.6–2581.4	≥2581.5
Protein (g)				
Men	≤68.5	68.6–84.3	84.4–101.2	≥101.3
Women	≤53.9	54.0–67.0	67.1–81.0	≥81.1
Fat (g)				
Men	≤39.1	39.2–54.4	54.5–72.4	≥72.5
Women	≤31.9	32.0–43.8	43.9–59.4	≥59.5
Carbohydrates (g)				
Men	≤404.9	405.0–473.9	474.0–550.4	≥550.5
Women	≤316.3	316.4–384.4	384.5–437.7	≥437.8
Dietary fiber (g)				
Men	≤7.7	7.8–9.8	9.9–12.2	≥12.3
Women	≤6.3	6.4–7.9	8.0–9.8	≥9.9
Vitamin C (mg)				
Men	≤48.7	48.8–68.2	68.3–86.0	≥86.1
Women	≤46.8	46.9–58.8	58.9–77.2	≥77.3
Carotene (mg)				
Men	≤738.7	738.8–1084.8	1084.9–1533.6	≥1533.7
Women	≤659.0	659.1–1005.0	1005.1–1300.9	≥1301.0
Vitamin A (μg)				
Men	≤94.6	94.7–181.8	181.9–313.0	≥313.1
Women	≤69.1	69.2–145.0	145.1–261.7	≥261.8
Vitamin E (mg)				
Men	≤19.7	19.8–24.7	24.8–31.6	≥31.7
Women	≤17.2	17.3–22.9	23.0–28.7	≥28.8